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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,397	03/09/2001	Muriel Moser	DECLE55.1CP2DV	7548

20995 7590 08/12/2003

KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER
EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
1644	17

DATE MAILED: 08/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/802,397	Applicant(s) Moser
	Examiner G.R. Ewoldt, Ph.D.	Art Unit 1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 2, 2003* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 3, and 5-28* is/are pending in the application.

4a) Of the above, claim(s) *27 and 28* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 3, and 5-26* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's election with traverse of the species, "dendritic cells" (DCs), in Paper No. 15, filed 6/02/03, is acknowledged. Applicant argues that the two species are not patentably distinct because DC precursors are defined in the specification as a subclass of DCs.

These argument are not found persuasive for the following reasons. DCs and DC precursors are separate and distinct cell types. The cells have different morphologies, are identified by different cell surface markers, and in particular, the cell types display different immunological properties. As such, restriction is proper.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 27 and 28 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 1, 3, and 5-26 read on the elected invention and are being acted upon.

3. Applicant's petition to correct inventorship by adding Inventors Pascal Mettens and Kris Thieleman to the application, filed 2/14/02, is granted.

4. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

A) Uninitialed changes in the residence address of Inventor Lespagnard have been made.

B) It is noted that the declaration has not been dated by Inventor Velu. However, MPEP 602.05 states that a new declaration will no longer be required in instances wherein the date of execution has been omitted.

5. Applicant has claimed the benefit of priority to U.S. Application Nos. 08/414,480, 08/625,507, 09/025,405, and 09/049,502.

In the instant application the term "dendritic cell" (DC) has been defined twice. At page 4 the term is defined to include "all non-B cells present in purified or enriched preparations of dendritic cells." It is also noted that at page 4 the term is disclosed as being interchangeable with the term "dendritic-like cell." DC is also defined at page 11 as "an isolated dendritic cell or its dendritic progenitor." Note that the second definition, while at first seeming to narrow the scope of the first, does not actually indicate that any of the "non-B cells" of the page 4 definition are intended to be excluded. Indeed, the page 11 definition can be interpreted as broadening the scope of the term to include dendritic progenitors not found in purified or enriched preparations. Accordingly, in the instant context, the term "dendritic cell" is considered to encompass all "non-B cells present in purified or enriched preparations of dendritic cells" as well as "dendritic progenitors" wherever they may be found.

Given the aforementioned definition of a DC the instant application cannot be granted the benefit of priority to the '480 parent application as said application does not disclose the broad definition of DC, i.e, "dendritic-like cells", found in the instant application. Additionally, the '480 application does not disclose DCs of lymphoid or myeloid origin, nor does it disclose a DC progenitor.

Regarding the '507 and '405 applications, at page 3, said applications disclose the broadly defined "dendritic-like cells" of the instant application. As the term"dendritic-like cell" is defined as being interchangeable with the term "dendritic cell", the instant application is granted the benefit of priority to the '507 application, i.e., a priority date of 3/29/96, with two exceptions. Claims 23 and 24 are drawn to DCs of lymphoid origin. Said DCs are not disclosed in the '507 nor '405 applications. Withdrawn Claims 27 and 28 are drawn to a DC progenitor. Said DC is not disclosed in the '507 nor '405 applications. Accordingly, Claims 23, 24, 27, and 28 are granted the priority date of the '502 application, 3/27/98.

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 3, and 19-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992).

Guo et al. teaches a plurality of hybrids (or hybridomas) comprising a bone marrow derived antigen-presenting B cell and a tumor cell (see particularly page 520, columns 2-3, 11.). The reference teaches that the hybrids comprise cells that express both tumor-specific antigens and the machinery for antigen presentation (see particularly page 518, column 1), that said hybrids are immunogenic, and that said hybrids induce a protective anti-tumor immune response that might otherwise "escape immune surveillance because they do not express signals that are essential for activation of the host immune system" (see particularly page 520, column 1 and page 518, column 1) upon administration to a subject.

The reference teaching differs from the claimed invention only in that it does not teach the use of a DC as the antigen presenting component of the hybrid.

Sornasse et al. teaches that , while both B cells and DCs are capable of inducing IL2 secretion *in vitro*, DCs induce a more vigorous response, including a Th1 response, *in vivo* (see particularly pages 16-17, Results). The reference teaches the superiority of DCs over B cells for *in vivo* use, "Our data emphasize the main role of DC in initiating primary responses in vivo" (see page 18, column 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a plurality of hybrids (or hybridomas) comprising a bone marrow derived antigen-presenting B cell and a tumor, said hybrids comprising cells that express both tumor-specific antigens and the machinery for antigen presentation, as taught by Guo et al., substituting a DC for the B cell in said hybrid, as taught by Sornasse et al., and administer said product to a subject for production of an anti-tumor response. One of ordinary skill in the art at the time of the invention would have been motivated to make said substitution because, while both B cells and DCs are capable of inducing IL2 secretion *in vitro*, DCs induce a more vigorous response, including a Th1 response, *in vivo*, as taught by Sornasse et al. "Our data emphasize the main role of DC in initiating primary responses in vivo". Note that the spleen cells of Guo et al. and Sornasse et al. would comprise an isolated DC as well as the only two known murine subtypes of DC, i.e., myeloid and lymphoid, both of which derive from bone

marrow.

8. Claims 5-10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992), as applied to Claims 1, 3, and 19-26 above, and in further view of U.S. Patent No. 5,851,756.

Guo et al. and Sornasse et al. have been discussed, supra. The references differ from the claimed invention in that they do not teach the induction of DC characteristics before using said hybrids or hybridoma, nor the induction of said characteristics using GM-CSF.

The '756 patent teaches the induction of DC characteristics using GM-CSF (see particularly Example I). The reference further teaches that DC exist in relatively small numbers in blood, thus the induction of DC (and thus, DC characteristics) in GM-CSF before use provides a method to increase the number of said DCs (see particularly column 4, line 63 - column 5, line 9).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a plurality of hybrids (or hybridomas) comprising a bone marrow derived antigen-presenting B cell and a tumor, said hybrids comprising cells that express both tumor-specific antigens and the machinery for antigen presentation, as taught by Guo et al., substituting a DC induced with GM-CSF before use, as taught by the '756 patent, for the B cell in said hybrid, as taught by Sornasse et al, and administer said product to a subject for production of an anti-tumor response. One of ordinary skill in the art at the time of the invention would have been motivated to make said substitution as set forth in section 7 above. One of ordinary skill in the art at the time of the invention would have been motivated to induce DC (and thus, DC characteristics) with GM-CSF before use because DC exist in relatively small numbers in blood, thus the induction of DC in GM-CSF before use provides a method to increase the number of said DCs, as taught by the '756 patent.

9. Claims 11-18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Guo et al. (1994, IDS) in view of Sornasse et al. (1992), as applied to Claims 1, 3, and 19-26 above, and in further view of U.S. Patent No. 5,637,483.

Guo et al. and Sornasse et al. have been discussed, supra. The references differ from the claimed invention in that they do not teach the treatment of the hybrids or hybridomas with

irradiation before using to prevent proliferation, nor do they teach administration by parenteral injection.

The '483 patent teaches the treatment of a tumor cell-containing anti-tumor vaccine with irradiation before using to prevent proliferation, and administration of said cell vaccine by parenteral injection (see particularly column 3, lines 65-67 and column 14, lines 3-4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce a plurality of hybrids (or hybridomas) comprising a bone marrow derived antigen-presenting B cell and a tumor, said hybrids comprising cells that express both tumor-specific antigens and the machinery for antigen presentation, as taught by Guo et al., substituting a DC for the B cell in said hybrid, as taught by Sornasse et al., treating the hybrids (or hybridomas) with irradiation before using, and administration of said cell vaccine by parenteral injection, as taught by the '483 patent, and administering said product to a subject for production of an anti-tumor response. One of ordinary skill in the art at the time of the invention would have been motivated to make said substitution as set forth in section 7 above. One of ordinary skill in the art at the time of the invention would have been motivated to treat the hybrids (or hybridomas) with irradiation before using to prevent proliferation, as taught by the '483 patent. One of ordinary skill in the art at the time of the invention would have been motivated to administer said hybrids (or hybridomas) by parenteral injection because this is the most well-known form of cell-based therapeutic administration.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805 The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
August 08, 2003